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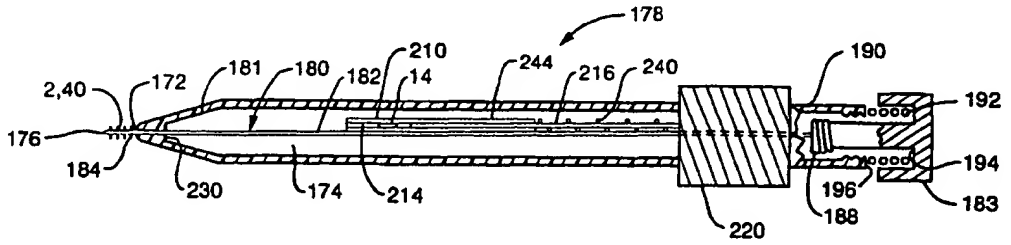
(54) Title: IMPLANT AND AGENT DELIVERY DEVICE



(57) Abstract: The present invention provides a system (178) for delivering a therapeutic agent in combination with an implanted device (2) to maximize a therapeutic benefit offered by each. Preferably, the therapeutic agent is contained within a solid matrix form such as a pellet or gel to facilitate its handling, and to regulate its rate of dissipation into the tissue after delivery. The implant device (2) is specially configured to receive retain the matrix but permit blood to interact with the matrix so that the agent can be released to the blood in, around the device, and the surrounding tissue. A delivery system (178) comprises an implant delivery device having an obturator (180) capable of piercing the tissue and an agent matrix delivery device (210) to place a matrix form, such as a pellet, into the interior of the implant (2) after it has been implanted. Preferably, the implant delivery device (178) and the matrix delivery device (210) are contained in one apparatus to facilitate delivery of the pellet into the embedded implant. The present invention is useful for treating tissue in any area of the body, especially ischemic tissue experiencing reduced blood flow. The present devices and methods are especially useful for treatment of ischemia of the myocardium. In treatment of the myocardium, the present implant device and matrix combination may be delivered surgically through the epicardium of the heart.

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IMPLANT AND AGENT DELIVERY DEVICE

Field of the Invention

The present invention relates to delivery of a therapeutic agent into tissue in combination with an implant device. Specifically, the agent is contained in a matrix form capturable within the implant device to provide the therapeutic advantages provided by both in a single treatment.

Background of the Invention

Tissue becomes ischemic when it is deprived of adequate blood flow. Ischemia causes pain in the area of the affected tissue and, in the case of muscle tissue, can interrupt muscular function. Left untreated, ischemic tissue can become infarcted and permanently non-functioning. Ischemia can be caused by a blockage in the vascular system that prohibits oxygenated blood from reaching the affected tissue area. However, ischemic tissue can be revived to function normally despite the deprivation of oxygenated blood because ischemic tissue can remain in a hibernating state, preserving its viability for some time. Restoring blood flow to the ischemic region serves to revive the ischemic tissue. Although ischemia can occur in various regions of the body, often myocardial tissue of the heart is affected by ischemia. Frequently, the myocardium is deprived of oxygenated blood flow due to coronary artery disease and occlusion of the coronary artery, which normally provides blood to the myocardium. The ischemic tissue causes pain to the individual affected.

Treatment of myocardial ischemia has been addressed by several techniques designed to restore blood supply to the affected region. A conventional approach to treatment of ischemia has been to administer anticoagulants with the objective of increasing blood flow by preventing formation of thrombus in the ischemic region.

Another conventional method of increasing blood flow to ischemic tissue of the myocardium is coronary artery bypass grafting (CABG). One type of CABG involves grafting a venous segment between the aorta and the coronary artery to bypass the occluded portion of the artery. Once blood flow is redirected to the portion of the coronary artery beyond the occlusion, the supply of oxygenated blood is restored to th area of ischemic tissue.

Early researchers, more than thirty years ago, reported promising results for revascularizing the myocardium by piercing the muscle to create multiple channels for blood flow. Sen, P.K. et al., "Transmyocardial Acupuncture - A New Approach to Myocardial Revascularization", *Journal of Thoracic and Cardiovascular Surgery*, Vol. 50, No. 2, August 1965, pp. 181-189. Although researchers have reported varying degrees of success with various methods of piercing the myocardium to restore blood flow to the muscle (which has become known generally as transmyocardial revascularization or TMR), many have faced common problems such as closure of the created channels. Various techniques of perforating the muscle tissue to avoid closure have been reported by researchers. These techniques include piercing with a solid sharp tip wire, or coring with a hypodermic tube. Reportedly, many of these methods produced trauma and tearing of the tissue that ultimately led to closure of the channel.

An alternative method of creating channels that potentially avoids the problem of closure involves the use of laser technology. Researchers have reported success in maintaining patent channels in the myocardium by forming the channels with the heat energy of a laser. Mirhoseini, M. et al., "Revascularization of the Heart by Laser", *Journal of Microsurgery*, Vol. 2, No. 4, June 1981, pp. 253-260. The laser was said to form channels in the tissue that were clean and made without tearing and trauma, suggesting that scarring does not occur and the channels are less likely to experience the closure that results from healing. U.S. Patent No. 5,769,843 (Abela et al.) discloses creating laser-made TMR channels utilizing a catheter based system. Abela also discloses a magnetic navigation system to guide the catheter to the desired position within the heart. Aita patents 5,380,316 and 5,389,096 disclose another approach to a catheter based system for TMR.

Although there has been some published recognition of the desirability of performing TMR in a non-laser catheterization procedure, there does not appear to be evidence that such procedures have been put into practice. U.S. Patent No. 5,429,144 (Wilk) discloses inserting an expandable implant within a preformed channel created within the myocardium for the purposes of creating blood flow into the tissue from the left ventricle.

Performing TMR by placing stents in the myocardium also is disclosed in U.S. Patent No. 5,810,836 (Hussein et al.). The Hussein patent discloses several stent embodiments that are delivered through the epicardium of the heart, into the myocardium and positioned to be open to the left ventricle. The stents are intended to maintain an open channel in the myocardium through which blood enters from the ventricle and perfuses into the myocardium.

Angiogenesis, the growth of new blood vessels in tissue, has been the subject of increased study in recent years. Such blood vessel growth to provide new supplies of oxygenated blood to a region of tissue has the potential to remedy a variety of tissue and muscular ailments, particularly ischemia. Primarily, study has focused on perfecting angiogenic factors such as human growth factors produced from genetic engineering techniques. It has been reported that injection of such a growth factor into myocardial tissue initiates angiogenesis at that site, which is exhibited by a new dense capillary network within the tissue. Schumacher et al., "Induction of Neo-Angiogenesis in Ischemic Myocardium by Human Growth Factors", *Circulation*, 1998; 97:645-650.

Summary of the Invention

The present invention provides a system for delivering a therapeutic agent in combination with an implantable device to maximize a therapeutic benefit offered by each. Preferably, the therapeutic agent is contained within a solid matrix form such as a pellet or gel to facilitate its handling and to regulate its rate of dissipation into the tissue after delivery. The implant device is specially configured to receive and retain the pellet but permit blood to interact with the pellet so that the agent can be released to the blood in and around the device and the surrounding tissue. A delivery system comprises an implant delivery device having an obturator capable of piercing the tissue and an agent matrix delivery device to place a matrix form, such as a pellet, into the interior of the implant after it has been implanted. Preferably, the implant delivery device and the pellet delivery device are contained in one apparatus to facilitate delivery of the pellet into th embedded implant.

The present invention is useful for treating tissue in any area of the body, especially ischemic tissue experiencing reduced blood flow. The present devices and methods are especially useful for treatment of ischemia of the myocardium. In treatment of the myocardium, the present implant device and pellet combination may be delivered surgically through the epicardium of the heart.

With specific agents and a particular configuration of the implant device, revascularization by angiogenesis and vessel recruitment can be encouraged in the ischemic tissue by use of the present invention. A wide range of therapeutic agents conducive to revascularization can be introduced via the matrix pellet including: growth factors; gene therapies or other natural or engineered substances that can be formed or added to the pellet. The pellet formation is well known in the medical field and typically comprises an inert powder pressed together to form a tablet or pill-like article.

The implant device also provides therapeutic benefit to the subject tissue in several ways. First the structure of the implant device provides an interior cavity within the tissue which permits blood to pool, mix with the agents of the matrix and coagulate. The coagulation occurs in and around the device as part of the coagulation cascade, that will eventually lead to new vessel formation and recruitment. Furthermore, the presence of a device in the moving tissue of a muscle such as the myocardium, creates an irritation or injury to the surrounding tissue which further promotes an injury response and the coagulation cascade that leads to new vessel growth. Additionally the implant causes a foreign body response, which causes inflammation attracting macrophages, which cause secretion of growth factors. Suitable implant devices should be flexible, define an interior, be anchorable within tissue and permit fluid such as blood to transfer between the surrounding tissue and the interior of the device. Examples of tissue implant devices are disclosed in pending U.S. Patent Application Serial Nos. 09/164,163, 09/164,173, 09/211,332 and 09/299,795, all of which are herein incorporated by reference. Delivery of therapeutic agents in a pellet form are discussed in pending U.S. Application Serial Nos. 08/993,586 and 09/116,313 and 09/159,834, all of which are herein incorporated by reference.

It is an object of the present invention to provide an agent delivery system that permits the delivery of an agent in combination with an implant device into tissue.

It is another object of the present invention to provide an implant device configured to retain an agent matrix form, such as a pellet, containing a therapeutic substance while it is implanted in tissue.

It is another object of the invention to provide a delivery method for sequentially delivering the implant device and a matrix containing a therapeutic substance that is relatively simple and effective.

It is another object of the present invention to provide a method for delivering an implant device and matrix containing a therapeutic agent that utilizes a simplified delivery device.

It is yet another object of the present invention to provide a dual step delivery system contained in one apparatus and associated method for sequentially delivering an implant then an agent suspending matrix form into the interior of the implant device placed in the tissue.

Brief Description of the Drawings

The foregoing and other objects and advantages of the invention will be appreciated more fully from the following further description thereof, with reference to the accompanying diagrammatic drawings wherein:

FIG. 1. is a side view of an implant device configured to accept a matrix;

FIG. 2. is a side view of an implant device containing a matrix;

FIG. 3 is a side view of an alternate embodiment of the tissue implant device;

FIG. 4 is a partial sectional view of the tissue implant device shown in FIG. 3;

FIG. 5A. is a partial sectional side view of an implant delivery device delivering an implant device;

FIG. 5B. is a partial sectional side view of the implant delivery device shown in FIG. 5A, delivering an agent carrying matrix into the implanted device;

FIG. 5C. is a detail of the distal tip of an implant delivery device shown in FIG 5B delivering an agent matrix into an implant.

Description of the Illustrative Embodiments

FIG. 1 shows a side view of an implant device 2 of the present invention. In a preferred embodiment the implant device 2 comprises a flexible helical coil having a plurality of individual coils 4 that define an interior 6. The device preferably has a distal region 8 and proximal region 10. The coils at the distal region 8 define a diameter that is smaller than that defined by the coils of proximal region 10. However, an agent carrying matrix, such as a pellet, may be inserted through proximal opening 12 into the proximal region 10 of the implant. The coils 4 of the distal region 8 are sized smaller than the pellet so that the pellet cannot slip out of the implant through the distal region. In the present application, proximal is understood to mean the direction leading external to the patient and distal is understood to mean a direction leading internally to the patient.

It should be noted that the agent carrying matrix may, but need not be a pellet form. A pellet may comprise a pill or tablet like article formed from inert substances compressed together; the substances are normally absorbable in the body. The pellet may be formed with a radiopaque seed to provide radiographic visibility of the implant location. In a preferred embodiment the pellet may have a generally cylindrical shape having a diameter on the order of .060 inch and a thickness of .028 inch.

FIG. 2 shows the implant device 2 implanted in tissue 3 and having captured with its interior 6 an agent carrying matrix 14, such as a pellet. The implant device maintains a cavity 18 within the tissue defined by the interior 6 of the device where the matrix may reside and blood may pool and mix with agents contained in the matrix 14. After the device is implanted in tissue, by steps which will be described in detail below, a tail 16 joined to the proximal end 22 of the device 2 serves to prevent the device from migrating out of the tissue. The tail may comprise a variety of configurations but should extend to have a profile that is greater than the diameter of the coils along the body 24 of the device. The tail projects into the tissue and is submerged beneath the surface 26 of the tissue 3 to prevent axial migration as well as rotation of the device, which could permit the device to move from the tissue location.

In one implant embodiment shown in FIG. 2, the pellet may be maintained in position within the interior 6 of the device 2 by reducing the diameter of the coils 4 of the proximal portion 10 of the device after the matrix 14 has been inserted. As mentioned above, the coils of the distal portion 8 are pre-formed to have a diameter that is smaller than the lateral extent of the pellet to prevent distal migration out of the device. The proximal portion coils 10 may be reduced in diameter by crimping by sterilized forceps after the implant device and matrix are delivered to the tissue. The reduced diameter coils of the proximal portion 10 and a distal portion 8 of the device leave a capturing portion 28 at the center of the device where the matrix will reside. The matrix may move slightly within this capturing portion 28 but will not migrate from either the proximal end 12 or distal end 13 of the device.

Preferably, the matrix is restrained in the implant by a close or a friction fit between the pellet and the inside diameter of the coils 4. So configured, there would be no clearance around an installed matrix and the implant device coils. The friction fit permits the matrix to be delivered into the device and retained without crimping the proximal coils behind the matrix to retain it, thereby eliminating an additional step after delivery. In this case, the implant device may be configured to have coils of approximately constant diameter. When a matrix, such as a pellet, is configured to have zero clearance with the inside diameter of the device, the pellet may be shaped to have a smaller profile distal end (leading edge) to be more easily insertable into the narrow opening of the device. An example of such a shape would be a cone shape pellet (not shown).

In treating the myocardium of the heart a preferred device length is on the order of approximately 7mm - 8mm. The device may be made from any implantable material such as surgical grades of stainless steel or a nickel titanium alloy. The filament of material from which the coils are formed may have any cross-sectional shape. A round filament may have a diameter on the order of .006 inch to .010 inch.

Alternatively, the implant may be formed from a filament having a rectangular cross-sectional shape. FIG. 3 shows an embodiment of a tubular implant device 40 formed from a filament 42 of rectangular cross-section such as a strand of flat wire. As shown in FIG. 4, the coil is formed so that the major cross-sectional axis 47 of the

rectangular wire is oriented at an acute angle to the longitudinal axis 50 of the coil 40. The orientation gives each turn 46 of the coil a projecting edge 44, which tends to claw into tissue to serve as an anchoring mechanism for the device. The implant device may have coils of substantially the same diameter sized to closely surround a matrix inserted into the implant interior. At least the most distal coil 54 should be wound to a smaller diameter that will frictionally engage the surface of the obturator delivery device as is discussed in detail below.

In addition to being retained by surrounding coils of the device, the matrix is supported in position within the device and within the capturing portion 28 by herniation points 20 of the surrounding tissue 3, as shown in FIG 2. After insertion of the device, surrounding tissue attempts to resume its previous position, collapsing around the individual coils 4 of the device and tending to herniate at points 20 through the spaces between the coils 4. The herniation points extending into the interior 6 of the device 2 engage the matrix 14 to help maintain it is position so that it does not migrate through either end or through the spaces between the coils 4.

With implants of the first embodiment in which the proximal coils are crimped after pellet delivery, it has proven desirable to have approximately .002 inch of clearance between the matrix and the inside diameter of the coils 4 in the larger coiled proximal region 10 (as well as the captured portion 28 -- after the proximal coils 10 have been crimped). Therefore, the preferable inside diameter of the coils 4 through a proximal region 10 is on the order of .065 inch. It has also been found desirable to have the restraining coils of small diameter, such as those at the distal portion 8, to be approximately .002 inch smaller in inside diameter than the diameter of the matrix. Therefore, the preferable inside diameter for distal coils 8 is approximately .055 to .056 inch. Likewise, it is preferable to have spacing between adjacent coils 4 of the implant device 2 to be no more than approximately .026 inch so that the matrix does not migrate through the space between the coils. In preferred implant embodiments having coils of constant diameter, the coils may define an inside diameter of approximately .061-.062 inch to closely surround a pellet of .060 inch diameter.

The implant devices 2 and 40 of the present invention are preferably delivered

to their intended tissue location surgically. FIGS. 5A - 5C show an example of a surgical delivery device 178 that may be used to deliver the implants into tissue such as that of the myocardium of the heart. The delivery device 178, shown in FIG. 5A, is, generally, a hollow rigid tubular structure formable or machined from a polymer that comprises an obturator 180 for delivering the implant and a matrix delivery tube 210 for delivering the agent matrix 14. Both are independently advanceable and retractable through the interior 174 of the device 178 to a distal port 172. The distal end 181 of the device 178 is shown in detail in FIG 5C.

The obturator includes a spring loaded main shaft 182, by which it can be gripped and manipulated by a threaded knob 183. The obturator 180 also includes a reduced diameter device support section 184 having a sharp distal tip 186 adapted to pierce tissue. The diameter of the shaft segment 184 is selected to fit closely within the interior 6 of the devices 2 and 40. Preferably, the obturator is configured so that the device is held onto the obturator only by a close frictional fit. The reduced diameter distal coil of an implant frictionally engages the support section 184. The proximal end of the segment 184 may terminate in a shoulder (not shown) formed at the junction of a proximally adjacent, slightly enlarged diameter portion 190 of the shaft. When the implant device 2 is mounted on the obturator 180, the proximal end of the device may bear against the shoulder. Alternatively, the distal end of the device support segment 184 may include a radially projecting pin (not shown) dimensioned to project and fit between adjacent turns of the coils 4. The pin engages the coils in a thread-like fashion so that after the assembly has been inserted into the tissue, the obturator 180 can be removed simply by unscrewing the obturator to free it from the implanted coil. Alternatively, the tip of the distal most coil of the implant may be deformed to project radially inward so as to catch a small receiving hole formed in the distal end of the support segment 184.

The matrix delivery tube 210 has slidable within its interior lumen 214 a push rod 216. The push rod is slidably controllable by slide 220, slidably mounted to the exterior of the body 200 of the device 178. A matrix pellet is sized to be retained in the lumen 214 of the delivery tube by the resilient force of the radially flexible tube against the matrix. The restraining force of the tube on the pellet can be easily over

come by advancement of the pushrod through the delivery tube 210. Advancement of slide 220 serves to move both the delivery tube 210 and pushrod 216 together in unison in the distal direction through the interior 174 until distal end 234 bottoms out against distal stop 236, an annular ridge encircling the exit port 172 of the device. After the distal end bottoms against the stop, distal movement of the delivery tube stops, but pushrod 216 keeps advancing distally to push matrix pellet 14 through the tube, out of the exit port 172 and into the interior 6 of the implanted device 2. Conical surface 238 captures the distal end 234 of the delivery tube and ensures alignment with the exit port 172.

Retraction spring 240 surrounds pushrod 216 and is restrained between proximal end 244 of delivery tube 210 and slide 220. The spring, therefore, causes delivery tube to advance distally with movement of slide and pushrod and compresses when delivery tube bottoms out and pushrod is advanced further. Advancement of the pushrod relative to the delivery tube serves to eject the matrix from the tube. After the matrix pellet 14 is pushed out of delivery tube, as shown in FIG. 5C, the slide may be released to permit pushrod to return to its retraced position. Delivery tube may be returned to its proximal position by proximal movement of the slide.

Prior to delivery of an implant and matrix, the obturator 180 is advanced distally to a delivery position, as shown in FIG. 5A, by screwing knob 183 so that knob threads 188 engage threaded sleeve 190. The delivery position of the obturator is reached after the threads of the knob have been advanced entirely through the threaded sleeve. In the delivery position, the support segment 184 of the obturator is advanced past the distal end 181 of the delivery device. In this configuration implant devices 2 or 40 may be manually loaded onto the support segment 184. Once mounted, the implant and underlying support segment 184 remain distal to the distal end 181 of the delivery device until the implant is placed in tissue and released

In use, the intended tissue location is first accessed surgically, such as by a cut-down method. In the delivery position of the delivery device, the implant may be delivered into tissue by manually advancing the delivery device to the tissue location. With application of a delivery force, the sharp tip 176 of the obturator pierces the tissue permitting the obturator and implant to be pushed inward into the tissue until

the distal end 181 of the device contacts the tissue indicating that the support segment 184 and implant have been fully inserted into the tissue. The advancement of the obturator and implant into the tissue may be aided by rotating the screw knob while applying the delivery force. The rotation may serve to provide a screwing action between the mounted implant and tissue being penetrated that will facilitate insertion. Retractable projecting barbs or vacuum suction may be added to the distal end of the delivery device to help maintain position of the distal end of the device on the tissue 26 during the matrix pellet delivery step that follows.

After the implant is placed in the tissue the obturator is disengaged by unscrewing the knob 183. Retraction spring 192 positioned around obturator shaft 182 so as to be biased between the inside surface 194 of knob 183 and proximal end 196 of body 200 is compressed while the obturator is advanced to the delivery position and thus serves to bias the obturator proximally so that threads 188 remain at the edge of engagement with threaded sleeve 190. Rotation of the knob 194 in the counter-clockwise direction causes the threads 188 to immediately engage the threaded sleeve, permitting the assembly to be unscrewed, which causes obturator to be rotated and moved proximally. Rotation and proximal withdrawal of the obturator also causes the implant to be released from frictional engagement with the support region 184 of the obturator. The implant remains in the tissue as the obturator is with drawn. Release of the threads 188 from threaded sleeve 190 permits spring to expand to quickly force the obturator shaft fully proximally to complete disengagement from the implant. The delivery tube then may be advanced to deliver the matrix. After the obturator is withdrawn, distal pressure is maintained on the body of the delivery device to ensure that the tapered portion 193 of the distal end 181 remains in the proximal end 12 of the implant to provide a pathway for the matrix delivery.

The delivery tube, preloaded with a matrix pellet may then be advanced distally by movement of the slide 220 as described above. During discharge of the matrix 14, the distal end of the device 181 should remain in position on the epicardial tissue surface 26 over the implant 2 to ensure tapered portion 193 remains in engagement with the implant 2, which ensures alignment of the exit port 172 with the interior 6 of the device 2, 40. After the matrix pellet is advanced into the interior of the implant,

the slide is moved proximally, aided by the retraction spring to withdraw the pushrod and delivery tube. The delivery device may then be with drawn from the site.

From the foregoing it should be appreciated that the invention provides an agent delivery system for delivering an agent carrying pellet and implant device in combination. The invention is particularly advantageous in promoting angiogenesis within an ischemic tissue such as myocardial tissue of the heart. The delivery system is simple to use and requires a minimum of steps to practice.

It should be understood, however, that the foregoing description of the invention is intended merely to be illustrative thereof and that other modifications, embodiments and equivalents may be apparent to those skilled in the art without departing from its spirit.

CLAIMS

1. A tissue implant comprising:

a porous body having an interior and proximal and distal ends;

wherein the proximal end of the implant is adapted to permit insertion of an agent carrying matrix into the interior of the implant after the implant has been placed in host tissue.

2. An implant as defined in claim 1 wherein the implant comprises a spring coil.

3. An implant as defined in claim 2 wherein the coil is substantially a constant diameter throughout its length.

4. An implant as defined in claim 2 wherein the coil is tapered, reducing in diameter from its proximal end to its distal end.

5. An implant as defined in claim 2 further comprising: a central region lying between the proximal and distal ends of the implant wherein coils that define the proximal and distal ends are of a smaller diameter than the coils of the central region.

6. An implant as defined in claim 5 wherein the coils that define the proximal region may be expanded temporarily to permit insertion of an agent carrying matrix into the interior of the implant, then released to return to a smaller diameter to retain the matrix within the interior of the implant.

7. An implant as defined in claim 5 wherein the proximal coils are compressed to a smaller diameter configuration after delivery of an agent substance carrying matrix into the interior of the implant through the proximal coils.

8. An implant as defined in claim 1 further comprising a therapeutic substance carrying matrix residing in the interior of the implant.

9. An implant as defined in claim 8 wherein the matrix is a solid form.

10. An implant as defined in claim 8 wherein the matrix is a pellet.

11. An implant as defined in claim 9 wherein the matrix is a gel.

12. An implant as defined in claim 10 wherein the pellet is substantially cylindrically shaped.

13. An implant as defined in claim 10 wherein the pellet is substantially cone shaped to facilitate entry into and frictional engagement with the interior of the implant.

14. A tissue implant and agent carrying matrix delivery system comprising:

a hollow tubular body defining an interior, distal end and distal port;

an obturator shaft having a proximal end, distal end, an implant device support section adjacent its distal end, a sharp distal tip and a handle at its proximal end for grasping and being advanceable through the interior of the body;

a matrix delivery tube, also advanceable through the interior of the body, having an interior lumen adapted to slidably receive an agent matrix, a push rod slidable through the lumen to advance the matrix through the tube and a distal end opened to the lumen;

a slide slidably mounted on the body and connected with the matrix delivery tube to advance the tube through the interior of the body with movement of the slide;

the obturator and matrix delivery tube being arranged so that each may be alternately advanced through the interior of the body to be placed in communication with the distal port.

15. A delivery device as defined in claim 14 further comprising:

a conical taper on the interior of the body near its distal end to help guide the obturator and matrix delivery tube to the distal port.

16. A delivery device as defined in claim 14 further comprising:

biasing members to bias the obturator and matrix delivery tube in retracted positions such that they do not extend through the distal port of the body.

17. A delivery device as defined in claim 14 wherein the device support section of the obturator is adapted to releaseably retain a tissue implant.

18. A delivery device as defined in claim 14 wherein the tubular body is rigid.

19. A method of treating tissue comprising:

delivering a tissue implant defining an interior into tissue;

inserting into the interior of the tissue implant a matrix carrying a therapeutic agent;

securing the matrix in the interior of the implant so that the therapeutic agent is permitted to be released to surrounding tissue.

20. A method of delivering an implant and agent carrying matrix into tissue comprising:

providing a tissue implant device defining an interior, an agent carrying matrix and a combination implant and agent matrix delivery device having proximal and distal ends and an interior;

loading the delivery device with a tissue implant and agent matrix;

positioning the delivery device adjacent tissue to be treated;

delivering the tissue implant device into tissue while maintaining communication of the interior of the implant with the interior of the delivery device;

delivering the agent matrix into the interior of the implant from the interior of the delivery device;

withdrawing the delivery device and leaving the implant and matrix in the tissue.

21. A method of delivering an implant and agent matrix as defined in claim 20 wherein the implant is secured after delivery of the agent matrix to prevent the matrix from leaving the interior of the implant while permitting the agent to be released into surrounding tissue.

22. A method of delivering an 6implant and agent matrix into tissue as defined in claim 20 wherein the implant is carried external to the delivery device and the matrix is carried internal to the delivery device during delivery.

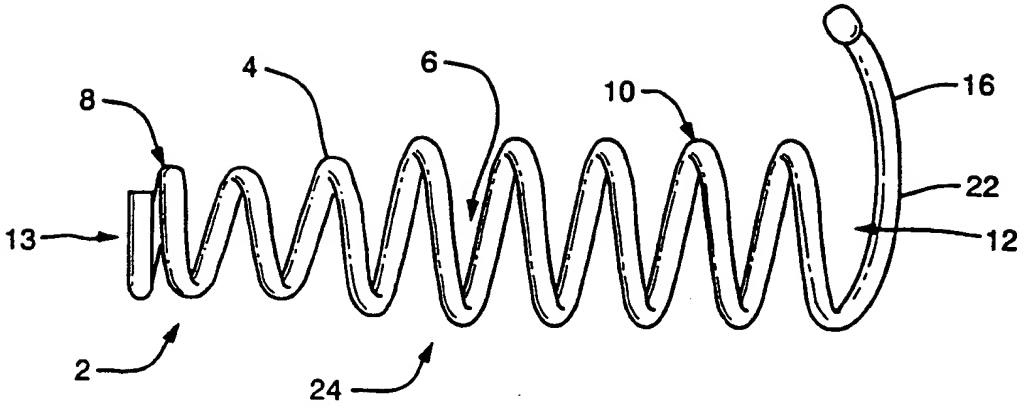

FIG. 1

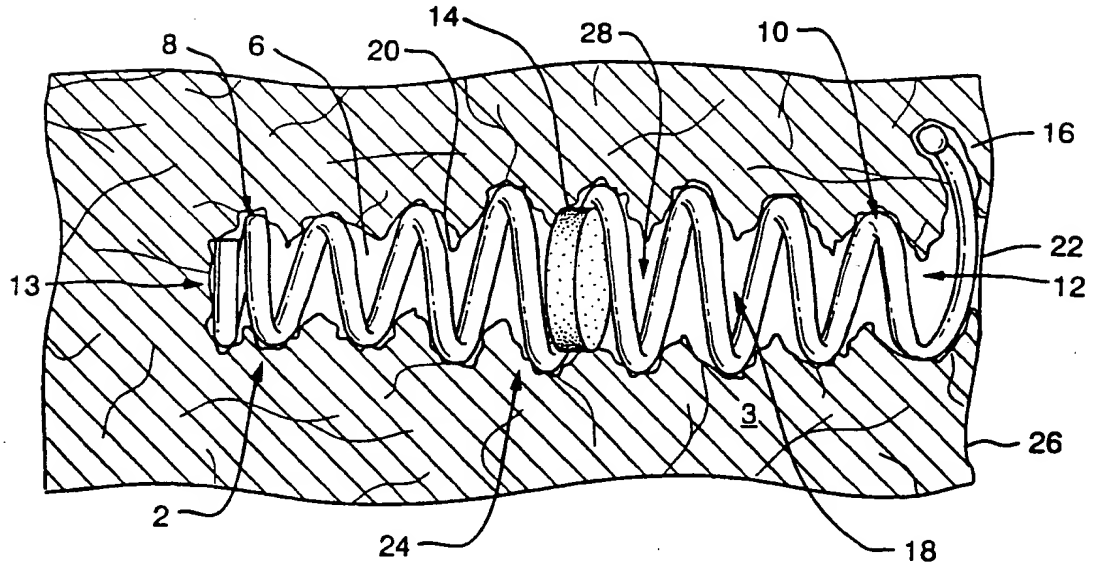

FIG. 2

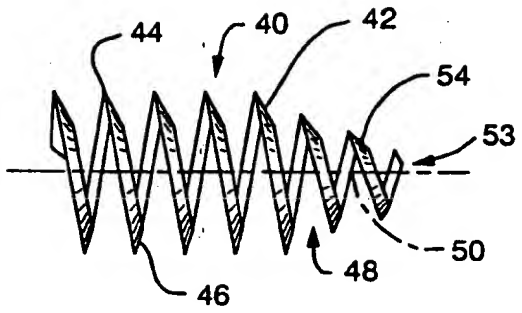

FIG. 3

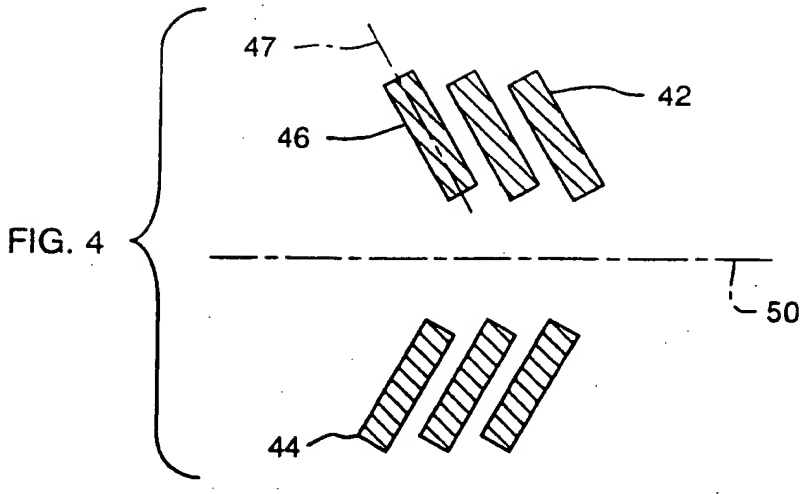

FIG. 4

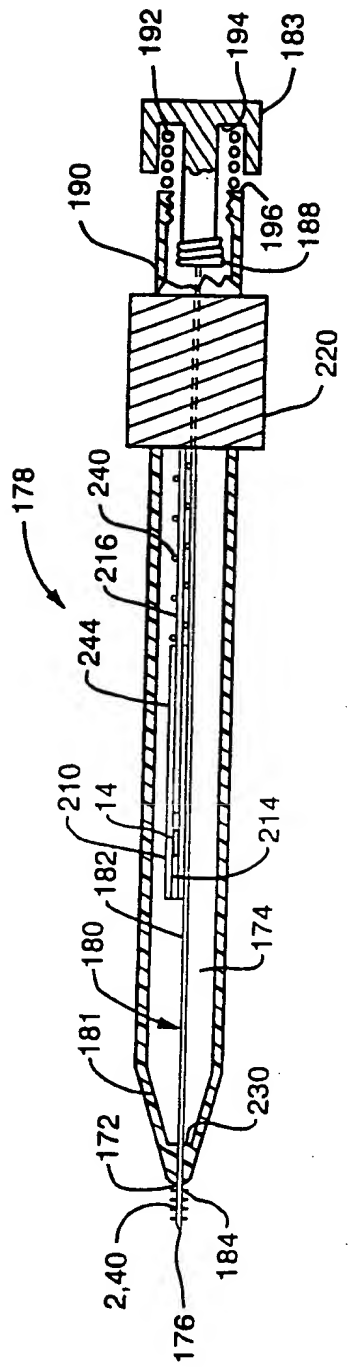
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FIG. 5A

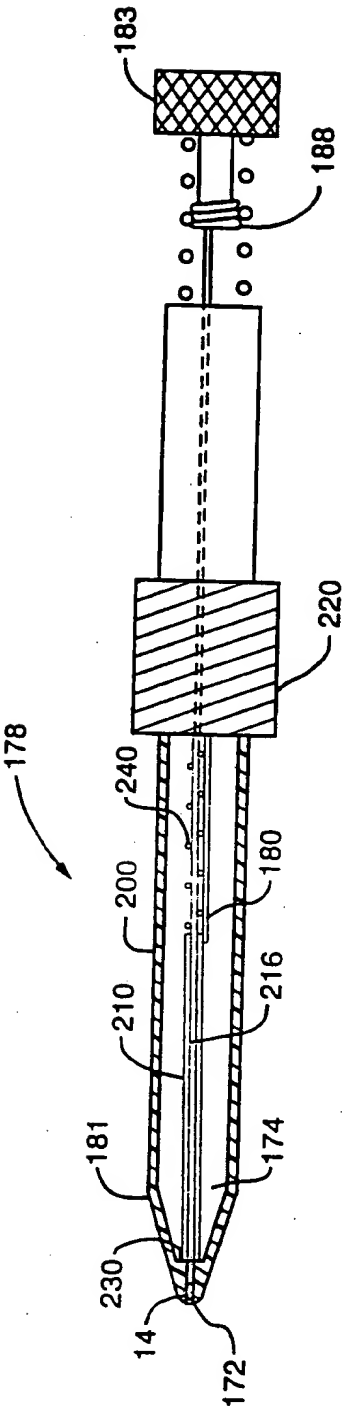
183
188
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FIG. 5B

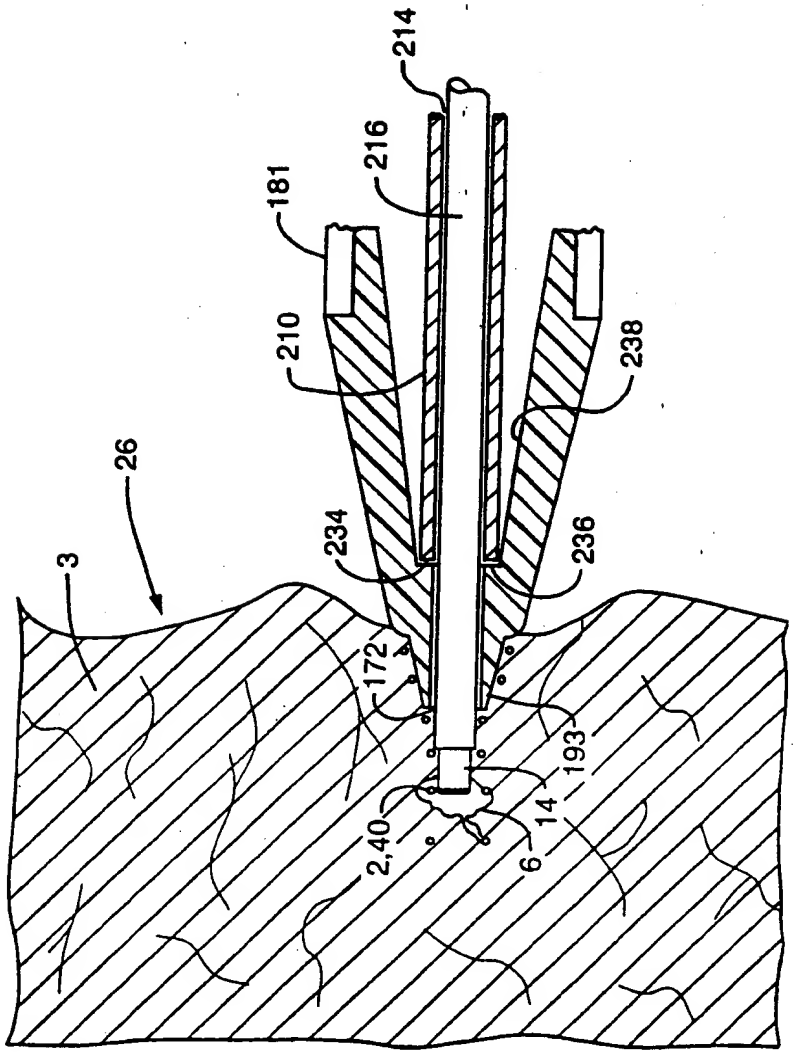

FIG. 5C

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/21215

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61F 2/06
US CL :623/1.42

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 623/1.42

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,891,108 A (LEONE et al.) 06 April 1999, entire publication.	1-22

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 SEPTEMBER 2000	04 OCT 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer DAVID J ISABELLA Telephone No. (703) 308-3060

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